REMARKS

Status of the Application and Claim Amendments

The instant Amendment is filed with a Request for Continued Examination, following the timely submission of a Notice of Appeal on January 26, 2006, and payment of all of the extension of time fees up until Saturday, August 26, 2006. Applicants respectfully request the entry of the RCE and above claim amendments under 37 C.F.R. § 1.114.

Claims 8, 10-17, and 20-30 are currently pending.

Claim 8 is amended to replace "active antithrombin III" with the "purified β isoform of antithrombin III." Similar amendments are made to claims 14, 15, and 17 for consistency. Claims 9, 18, and 19 are canceled without prejudice or disclaimer. The amendments are supported by the application as a whole, which describes the separation of the α and β isoforms of antithrombin III and subsequent purification and testing of each separate form, as well as antithrombin III concentrates. (See, for instance, the application at page 3, line 17, through to page 5, line 15, and the working examples. See also, for example, Figure 1, which shows the different activities of the purified α and β isoforms.)

New claims 20-28 follow the same pattern as amended claims 8 and 10-17, but claim "purified α isoform of antithrombin III." New claims 29 and 30 recite a "mixture of purified α isoform and β isoform." Support for those claims may be found in the application as a whole, for example, at the same locations as provided above: at page 3, line 17, through to page 5, line 15, and the working examples and Figure 1, as well as at page 8, lines 25-27, and in original claim 3.

Thus, the amendments and new claims do not include new matter and may be immediately entered.

The Pending Claims Are Novel under 35 U.S.C. § 102

Rejection of claims 8-15 as anticipated by O'Reilly (U.S. 2002/0076413) in light of Webster's Dictionary definition of "active"

The Office first rejects claims 8-15 as allegedly anticipated by a published patent application to O'Reilly, in light of a definition of the word "active" from the 1994 Webster's Dictionary. (Office Action at pages 2-3.)

That rejection is moot in light of amended claim 8. Claim 8 now recites a "purified β isoform of antithrombin III" and no longer recites the word "active." Thus, the Office's assertions about the scope of the term "active antithrombin III" and the Office's discussion about whether or not that term could encompass O'Reilly's teachings are inapposite.

In any event, in order to anticipate a claim, a single publication must teach, either expressly or inherently, each and every element of the claim, in as complete detail as contained within the claim. M.P.E.P. § 2131; *Verdegaal Bros. v. Union Oil Co. of Calif.*, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987); *Richardson v. Suzuki Motor Co.*, 9 U.S.P.Q.2d 1913, 1920 (Fed. Cir. 1989). O'Reilly cannot anticipate any of claims 8-18 or 20-29 because it does not teach or suggest administering a "purified β isoform of antithrombin III," a "purified α isoform of antithrombin III," or a mixture of those forms.

For example, O'Reilly administers a cleaved form of antithrombin III called "R-AT3." (See O'Reilly at ¶¶ 0007, 0041, 0090, and Figure 1.) O'Reilly also mentions another purified form called "L-AT3." (O'Reilly at ¶¶ 0042 and 0090, and Figure 1.)

O'Reilly expressly points out that both the R-AT3 and the L-AT3 forms are not active as serine protease inhibitors. (O'Reilly at ¶ 0041-0042.) In contrast, the instant claimed isoforms of antithrombin III both "inhibit proteases such as thrombin and factor XIa." (Specification at page 3, lines 7-10.) Applicants' specification also states that O'Reilly's forms have different properties than the claimed α and β isoforms. (Specification at page 2, lines 29-33, and at page 3, lines 6-34.) Because O'Reilly's forms of antithrombin III have different biological activities than the claimed forms, they are inherently different. Thus, Applicants request the withdrawal of this rejection.

Rejection of claims 8, 10, 13, 15, and 17-19 as anticipated by Romisch et al. (U.S. Patent No. 6,399,572) in light of Webster's Dictionary

The Office next rejects the claims over the Romisch patent, again using a 1994 Webster's Dictionary definition of the word "active." (Office Action at pages 3-4.) Again, because of the claim amendments, which remove the word "active," this rejection is also moot.

Romisch does not teach a "purified β isoform of antithrombin III," or a "purified α isoform of antithrombin III," or a mixture of the two, as the instant independent claims require. For that reason alone, it cannot anticipate any of the instant claims. Nor does it suggest purifying either of the above isoforms. Hence, Applicants request the withdrawal of this rejection.

Rejection of claims 8-16 as anticipated by Green et al. (U.S. Patent No. 6,593,291) in light of Webster's Dictionary

Next, the Office rejects claims 8-16 over Green, again using the 1994 Webster's Dictionary to define the term "active," which is no longer in the pending claims. (Office Action at pages 5-6.) Because of the instant amendments, this rejection is also moot.

Like Romisch, Green does not teach a "purified β isoform of antithrombin III," or a "purified α isoform of antithrombin III," or a mixture of the two, as the instant independent claims recite. Instead, Green discloses a vast array of compositions seemingly including every protein involved in the blood coagulation pathway, every protein that binds or affects the activity of tissue factor, as well as peptide fragments derived from that large multitude of proteins. For example, Green describes administering "TFPI, protein S, protein Z, protein Z inhibitor, protein C, activated protein C, protein C inhibitor, prothrombin, group II secretory phospholipase A2, complement protein C4b, protease nexin-1, beta2-glycoprotein 1, and serpins anticoagulants (such as antithrombin and heparin cofactor II) and inhibitors of factors TF, TF/VIIa, VIIa, Xa." (Green at col. 4, lines 26-35.) Given those vague and general teachings, Green cannot anticipate any of the instant pending claims and Applicants request that this rejection be withdrawn.

Rejection of Claims 8-10, 13, and 15 as anticipated by Emerson

Finally, the Office rejects claims 8-10, 13, and 15 over an article by Emerson (*Blood Coag. Fibrinolys.* 5(1): S37-S45 (1997)). (Office Action at 6-7.) Because of the instant amendments, this rejection is moot as well.

But in any case, like Romisch and Green, Emerson does not teach a "purified β isoform of antithrombin III," or a "purified α isoform of antithrombin III," or a mixture of the two, as the instant claims recite. Instead, it merely discusses the antithrombin III protein in general. Therefore, Emerson also cannot anticipate any of the instant pending claims and Applicants request that this rejection be withdrawn.

In summary, none of the four documents above: O'Reilly, Romisch, Green, and Emerson, refer to the specific, purified protein isoforms claimed in the instant claims 8-18 and 20-29. Because all of those documents fail to teach those required claim elements, none of the above rejections presents a *prima facie* case of anticipation and all four rejections must be withdrawn.

The Pending Claims are Nonobvious under 35 U.S.C. § 103

Rejection of Claims 8, 10, and 16 as obvious over O'Reilly in view of Antunes et al. and Webster's Dictionary

The Office also asserts that claims 8, 10, and 16 are rendered obvious by O'Reilly in view of Antunes et al. and the 1994 Webster's Dictionary definition of the word "active." (Office Action at 7-8.) Because of the above claim amendments, this rejection, like the others discussed previously, is moot.

In any event, the rejection is not a *prima facie* case of obviousness.

There are three distinct requirements for a *prima facie* case of obviousness. First, the references must teach or suggest every claim element. M.P.E.P. §§ 2142 and 2143.03. As described in a previous section, O'Reilly does not teach purified α or β isoforms of antithrombin III or mixtures thereof as the instant independent claims require. Antunes does not rectify that problem because it does not even mention

antithrombin III protein whatsoever. Thus, the combination of O'Reilly and Antunes does not teach all of the instant claim elements. For that reason alone, the rejection must be withdrawn.

But the combination also fails the other requirements for a *prima facie* case of obviousness. The second requirement is a motivation to modify or combine the teachings of the cited references in order to arrive at the invention as claimed. M.P.E.P. §§ 2143 and 2143.01. The motivation must come from the references themselves or from the knowledge generally available to one of ordinary skill in the art; not from the applicant's disclosure. *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991); M.P.E.P. § 2142. In other words, one takes the view of a person of ordinary skill in the art who knows nothing about the applicant's invention. Under that standard, there can be no motivation to combine O'Reilly with Antunes to arrive at the instant claims. Indeed, O'Reilly distinctly teaches away from using purified α or β isoforms of antithrombin III or mixtures thereof, as the instant claims recite, because it explains that forms of antithrombin III that retain protease activity, as those forms do, are undesirable. Instead, it teaches that the R-AT3 and L-AT3 forms, which do not have protease activity, should be administered. Antunes, because it does not even mention antithrombin III, cannot possibly bridge that fundamental gap in O'Reilly's teachings.

The third requirement for a *prima facie* case of obviousness is a reasonable expectation of success in performing the combined teachings as claimed, based on the prior art. M.P.E.P. § 2142. The combination of O'Reilly and Antutes likewise fails this test because O'Reilly strongly teaches away from using any protease-active antithrombin III isoform, as noted above. Based on O'Reilly's results, one would not

expect that the intact, active, purified isoforms which Applicants claim to successfully affect angiogenesis or arteriogenesis. Again, Antunes cannot overcome that deficiency in O'Reilly because it does not even discuss antithrombin III.

Therefore, because the combination of O'Reilly and Antunes fails all three requirements of a *prima facie* case, while the Webster's Dictionary entry is not applicable, Applicants submit that this rejection must be withdrawn.

Rejection of Claims 8, 10, and 16 as obvious over Green et al. in view of Antunes et al. and Webster's Dictionary

The Office also rejects claims 8, 10, and 16 over Green in combination with Antunes and the 1994 Webster's Dictionary definition of "active." (Office Action at 8-9.) Again, in light of the claim amendments, this rejection is also moot.

Further, it also fails the same three-part test as the combination of O'Reilly and Antunes described above. Like O'Reilly, Green does not teach using purified β or α isoforms of antithrombin III or mixtures thereof. Instead, Green at col. 4, lines 26-35, very generally refers to administering any of a large number of different types and classes of proteins. Later on in the document, Green comments that a cleaved form of antithrombin III should be used. (See col. 18, working example 4.) In particular, Green states that "it is likely that complexing with factor Xa and/or proteolytic cleavage of [a] limited number of residues of AT3 may enhance the anti-angiogenic activity of AT3." (Green at col. 18, lines 46-49.) In other words, like O'Reilly, Green is suggesting that a cleaved form of antithrombin III rather than an intact form such as purified β or α isoform should be administered.

Thus, Green teaches away from using an intact, purified β or α isoform. Antunes cannot rectify that problem with Green because does not even mention antithrombin III. Hence, the combination of Green and Antunes does not teach or suggest all of the instant claim elements. In addition, there can also be no motivation to combine those documents to arrive at Applicants claims reciting particular, purified isoforms of antithrombin III, and no reasonably expectation of success in administering such purified forms and mixtures thereof.

For those reasons, the rejection over Green and Antunes must also be withdrawn.

In view of the foregoing amendments and remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any required fees not found herewith to our deposit account 06-0916.

Respectfully submitted,

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Dated: August 25, 2006

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Attachments: **RCE Form**
Petition for Five (5) Month Extension of Time
Information Disclosure Statement and PTO SB/08 Form